Award ID: RP160512

Project Title:

Integrin-mediated IL-18 signaling in the prevention and treatment of inflammation-associated colorectal cancer

Award Mechanism: Individual Investigator

Principal Investigator: Dube, Peter

Entity:

The University of Texas Health Science Center at San Antonio

Lay Summary:

Worldwide colorectal cancer is the third and fourth most common cancer-related cause of death for women and men respectively. There are many factors that contribute colorectal cancer but uncontrolled inflammation is a major risk factor. This partially explains why people with inflammatory bowel disease, IBD, are at a significantly higher risk of developing colorectal cancer. A significant advance in our understanding of the link between IBD and colorectal cancer was made a few years ago when it was discovered that a set of genes that regulate inflammation through a cellular machine called the inflammasome, could protect against both IBD and colorectal cancer. The inflammasome leads to the production of a signaling protein called IL-18 in the intestine that is important for repairing the gut after inflammatory insult and has an overall antiinflammatory effect on the gut. We recently defined the signaling pathways leading to inflammasome activation and IL-18 production in the cells that line the intestine called intestinal epithelial cells. In a major step towards harnessing IL-18 for treating IBD and colorectal cancer, we engineered bacteria that can induce IL-18 from intestinal epithelial cells. In the current application we propose to refine our understanding of IL-18 mediated responses in intestinal epithelial cells. Further, we will test if our engineered bacterial strains can be used to modify the microbial composition of the gut as a treatment for IBD and a preventative for colorectal cancer. If successful, this application represents a new approach for developing simple and cost effective methods for treating IBD and preventing colorectal cancer.